



MI FluFocus

Influenza Surveillance and Avian Influenza Update

**Bureau of Epidemiology
Bureau of Laboratories**



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New updates in this issue:

- **Michigan:** Influenza activity remains at baseline summer levels of little to no activity.
 - **National:** New research studies shed light on potential new antiviral medications.
 - **International:** Active but declining transmission of 2009 H1N1 persists in limited areas of the tropics.
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******2009 Influenza A (H1N1) virus Updates******

Please continue to reference the MDCH influenza website at www.michigan.gov/flu for additional 2009 H1N1 information. Local health departments can find guidance documents in the MI-HAN document library. In addition, additional laboratory-specific information is located at the Bureau of Laboratories H1N1 page at http://www.michigan.gov/mdch/0,1607,7-132-2945_5103-213906--,00.html.

******Influenza Surveillance Reports******

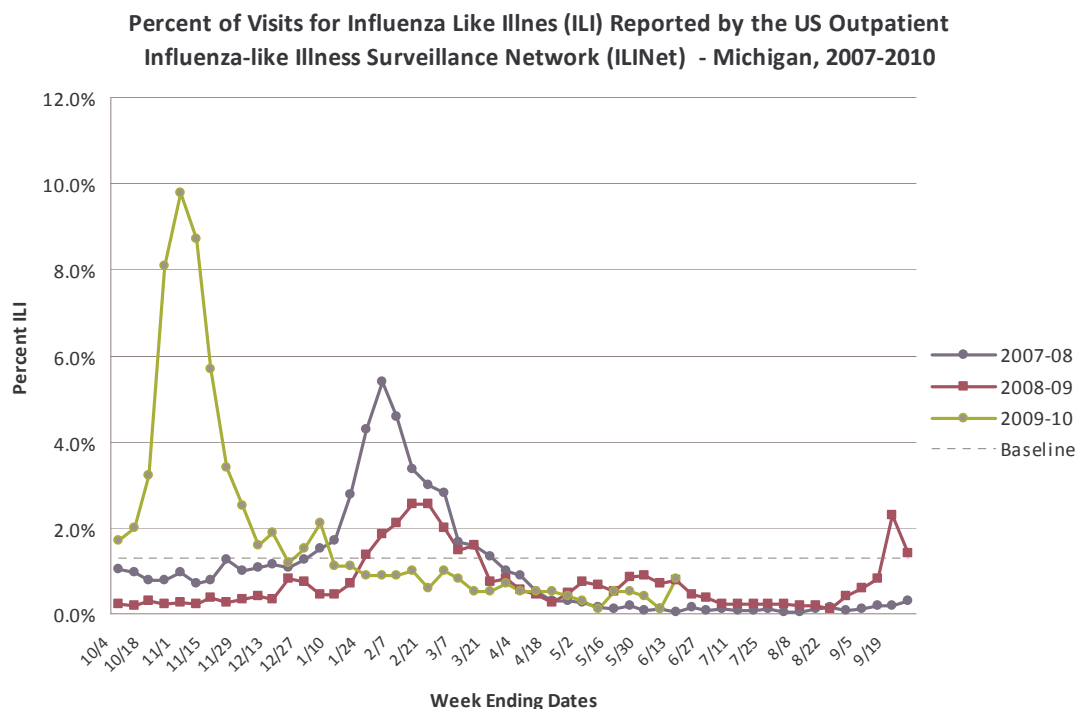
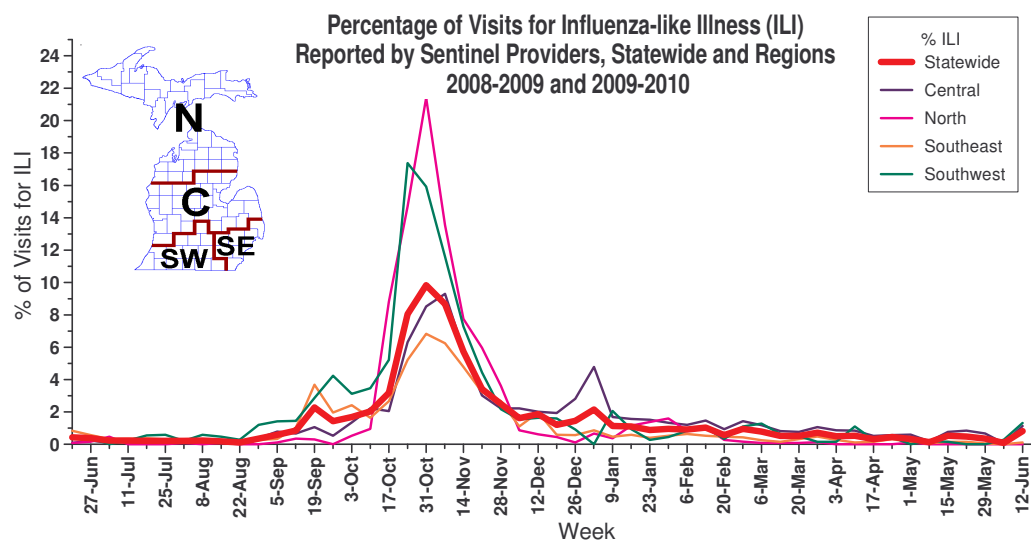
Michigan Disease Surveillance System: MDSS data for the week ending June 12th showed that aggregate influenza case reports decreased, while individual influenza and 2009 novel influenza reports remained near the previous week's reported levels of little to no activity. Aggregate influenza cases are similar to levels seen during the same reporting period in 2009. Individual influenza reports are dramatically lower than data from the same reporting period last year, which is attributable to the first wave of pandemic H1N1 influenza in 2009.

Emergency Department Surveillance: For the week ending June 12th, emergency department visits from constitutional and respiratory complaints were comparable to the previous week's levels, although respiratory complaints have decreased slightly over the past month. Constitutional complaints are moderately lower compared to the same reporting period last year, while respiratory complaints are similar. During the past week, there were five constitutional alerts in the C(3) and N(2) Influenza Surveillance Regions, and there were four respiratory alerts in the N(2), C(1), and SW(1) Influenza Surveillance Regions.

Over-the-Counter Product Surveillance: During the week of June 6-12, OTC product sales of thermometers, pediatric electrolytes, cough/cold aides, and chest rubs remained similar to last week's levels. All indicators are consistent with levels seen at this time last year, except for thermometer sales, which are slightly lower.

Sentinel Provider Surveillance (as of June 17): During the week ending June 12, 2010, the proportion of visits due to influenza-like illness (ILI) slightly increased to 0.8% overall. Thirty-six patient visits due to ILI were reported out of 4,429 office visits. Only fifteen sentinel sites provided data for this report, which limits the validity of the slight increase. Activity increased in three surveillance regions: Central (1.1%), Southeast (0.1%) and Southwest (1.3%); and there continued to be no ILI activity in the North region. Please note that these rates may change as additional reports are received.

As part of pandemic influenza surveillance, CDC and MDCH highly encourage year-round participation from all sentinel providers. New practices are encouraged to join the sentinel surveillance program today! Contact Cristi Carlton at 517-335-9104 or CarltonC2@michigan.gov for more information.



Laboratory Surveillance (as of June 12): During May 30 - June 12, MDCH Bureau of Laboratories identified no influenza isolates. For the 2009-2010 season (starting on October 4, 2009), MDCH BOL has identified 610 influenza isolates:

- 2009 Influenza A (H1N1): 609
- Influenza B: 1

Six sentinel laboratories reported for the week ending June 12, 2010. All laboratories (SE, SW, C, N) reported no influenza A or B positive test results, with very few specimens being tested.

Michigan Influenza Antigenic Characterization (as of June 17): One 2009 H1N1 influenza A virus from Michigan has undergone further characterization at the CDC. This virus was characterized as A/California/07/2009 (H1N1)-like, which is the recommended strain for the H1 component of the 2010-11 Northern Hemisphere vaccine.

Michigan Influenza Antiviral Resistance Data (as of June 17): Results are currently not available for antiviral resistance at CDC for the 2009-2010 season.

Antiviral resistance testing takes months to complete and cannot be used to guide individual patient treatment. However, CDC has made recommendations regarding the use of antivirals for treatment and prophylaxis of influenza. The guidance is available at <http://www.cdc.gov/H1N1flu/recommendations.htm>.

Influenza-Associated Pediatric Mortality (as of June 17): Five 2009 H1N1 influenza-associated pediatric mortalities (SE(3), SW, N) have been reported to MDCH for the 2009-2010 influenza season.

***CDC has asked states for information on any pediatric death associated with influenza. This includes not only any pediatric death (<18 years) resulting from a compatible illness with laboratory confirmation of influenza, but also any unexplained pediatric death with evidence of an infectious process. Please immediately call MDCH to ensure proper specimens are obtained. View the complete MDCH protocol online at http://www.michigan.gov/documents/mdch/ME_pediatric_influenza_guidance_v2_214270_7.pdf.

Influenza Congregate Settings Outbreaks (as of June 17): Seven congregate setting outbreaks with confirmatory novel influenza A H1N1 testing (2SE, 3 SW, 1C, 1N), and three outbreaks associated with positive influenza A tests (2C, 1N) have been reported to MDCH for the 2009-2010 influenza season. These are 8 school facilities and 2 long term care facilities. Human metapneumovirus was confirmed in one outbreak in a long term care facility (SW) in February. Adenovirus was confirmed from one outbreak in an elementary school (SW) in May.

During fall 2009, 567 influenza-related school and/or district closures in Michigan (Public Health Preparedness Region 1 - 55, Region 2N - 4, Region 2S - 8, Region 3 - 54, Region 5 - 153, Region 6 - 100, Region 7 - 109, Region 8 - 84) were reported.

National: To access previous Center for Disease Control and Prevention weekly surveillance reports, visit <http://www.cdc.gov/flu/weekly/fluactivity.htm>.

International (WHO Pandemic update 104 [edited], June 11): Active but declining transmission of pandemic influenza persists in limited areas of the tropics, particularly in SE Asia and the Caribbean. As countries of the temperate southern hemisphere enter winter, only sporadic influenza activity has been detected so far, except in Chile and Uruguay, both of which have recently reported small numbers of pandemic influenza virus detections. Although seasonal influenza B viruses have been the predominant type of influenza virus circulating worldwide since the end of February 2010, there have been increasing but low level detections of seasonal H3N2 viruses, particularly in South America and in East Africa.

In the tropics of the Americas, overall pandemic influenza activity is low, however, both seasonal H3N2 and type B viruses are actively circulating in parts of tropical South America. Active but declining transmission of pandemic influenza continues to be detected primarily in Cuba. Since early 2010, pandemic influenza has circulated at low levels in Costa Rica. Sporadic detections of pandemic influenza continue to be reported in Brazil. During the most recent reporting week, both Brazil and Venezuela reported regional spread of influenza activity associated with an increasing trend of respiratory diseases. In Venezuela, recent influenza activity (which began during early May 2010) has been predominantly due to circulating seasonal influenza A viruses. In Bolivia, circulation of seasonal influenza viruses, predominantly type B, was observed between March and May 2010 and now appears to be subsiding.

In Asia overall pandemic influenza transmission remains low, except in parts of tropical South and SE Asia, particularly Singapore, Malaysia, and Bangladesh. In Singapore, overall levels of ARI remained slightly below epidemic threshold and the proportion of respiratory samples testing positive for pandemic influenza increased slightly to 34%. In Malaysia, limited data suggests that pandemic influenza transmission has begun to decline since plateauing during May 2010. In Bangladesh, there has been stable persistent low level co-circulation of pandemic and influenza B since March 2010. Sporadic detections of pandemic influenza continued to be reported across other parts of Asia. In East Asia, overall activity remains low, however, seasonal B viruses continue to circulate at low and declining levels.

In Sub-Saharan Africa, pandemic influenza virus continued to circulate at low levels in parts of West Africa, most notably in Ghana. During the most recent reporting week, 13% of all respiratory samples tested positive for pandemic influenza virus in Ghana. Small but significant numbers of seasonal H3N2 viruses have been detected in Kenya and Tanzania since late May 2010.

Overall, in the temperate regions of the northern hemisphere, pandemic influenza viruses have been detected only sporadically during the past month. In the temperate southern hemisphere, only two countries, Chile and Uruguay, have recently reported small numbers of pandemic influenza virus detections. In Chile, there was low level geographically limited circulation of pandemic influenza virus during May 2010; 3.4% of respiratory samples tested positive for pandemic influenza virus during the last week of May 2010. Of note, in Uruguay, 11 (44%) of 25 samples tested positive for pandemic influenza during the most recent reporting week (the last week of May 2010); however, the corresponding intensity of respiratory diseases in the population is not yet known. Other respiratory viruses, most notably RSV,

are known to be circulating in Chile and Argentina. There have been no recent detections of pandemic influenza virus in South Africa. In New Zealand and Australia, overall levels of ILI remain low; only sporadic detections of seasonal and pandemic influenza viruses have been recently reported in Australia.

Weekly reporting of influenza activity to the CDC has concluded for the 2009-2010 season.

For those interested in additional influenza vaccination and education information, the MDCH *FluBytes* is available at http://www.michigan.gov/mdch/0,1607,7-132-2940_2955_22779_40563-125027--,00.html.

Novel Influenza Activity and Other News

WHO Pandemic Phase: Phase 6 – characterized by increased and sustained transmission in the general population. Human to human transmission of an animal or human-animal influenza reassortant virus has caused sustained community level outbreaks in at least two WHO regions.

National, Research (Mount Sinai School of Medicine press release, June 2): Researchers at Mount Sinai School of Medicine have discovered a novel component of the influenza virus that may be the key to disabling the virus's ability to replicate itself and to developing a universal anti-viral treatment. The findings were published June 1 online in Proceedings of the National Academy of Sciences.

The influenza A virus is encoded by eight individual single-stranded segments of RNA. Each segment must serve as the material for both making protein and new segments, processes called transcription and replication. As each strand must perform both functions, it is imperative that the virus prioritize these processes, starting with transcription and then switching to replication.

Mount Sinai researchers have, for the first time, identified a small-viral RNA (svRNA), derived from the virus, that is integral to the switch from transcription to replication. Inhibiting svRNA from making this switch would stymie replication and thus slow or halt the spread of the virus. Because segment ends and replication strategies used for influenza B and C are similar to those of influenza A, this discovery can lead to a universal treatment for people suffering from the disease. It would also be effective against the H1N1 swine flu virus.

"The implications of this study are very exciting," said Benjamin tenOever, PhD, Assistant Professor of Microbiology at Mount Sinai School of Medicine and corresponding author of the study. "While each segment encodes different viral products, the svRNAs remain consistent, both between segments and across viral strains. If we can block the availability of svRNA we can inhibit the switch to replication, thereby stopping viral spread. As an added bonus, if the virus remains stuck in transcription, it will continue to produce proteins, ultimately strengthening the antibody response." The small RNA component was originally identified through a process called deep sequencing. This revolutionary new technique allows scientists to obtain millions of small RNAs from cells in a completely unbiased fashion. The technique was applied to lung cells infected with influenza A virus and ultimately led to the discovery of the first small RNA component ever identified from this family of viruses.

"Questions remain about exactly how the svRNAs function," said Dr. tenOever. "We're also hoping to engineer a means of delivering RNA-based antagonists into the body's system as a means of inhibiting svRNA function. We're still a few years off from solving the entire puzzle. However, by finding this one piece, a universal treatment for all strains of influenza is within reach of becoming a reality."

National, Research (Reuters Health News [edited], June 4): Researchers reported on Thursday that 2 extra mutations set the stage for the seasonal influenza virus to evolve into a form that now resists 3 of the 4 drugs designed to fight it. Their study, published in Science, provides a way for scientists to keep an eye out for dangerous mutations in new flu viruses, including the ongoing pandemic of H1N1 swine flu.

Only 4 drugs are on the market to treat flu and 2, the adamantines, are useless against virtually all circulating strains because the viruses have evolved resistance. Tamiflu, known generically as oseltamivir, is the current drug of choice. It comes as a pill. An inhaled drug that works in a similar manner is called Relenza, or zanamivir generically. Both can help reduce flu symptoms if taken quickly and can keep the most vulnerable patients out of the hospital, or keep them alive if they are severely ill. But 2 years ago the common circulating strain of seasonal H1N1 developed resistance to Tamiflu.

Doctors were surprised, because the mutation that help the virus evade the effects of Tamiflu also usually made it a weak virus that did not infect or spread well. "People have known about this H274Y mutation for

over a decade, but the mutation seemed to interfere with the virus's ability to replicate and be transmitted," Jesse Bloom of the California Institute of Technology, who led the study, said. "Something happened to make the Tamiflu-resistant virus capable of replicating and spreading like wild-type viruses."

Bloom and Dr David Baltimore, an expert on AIDS and on the genetic functions of cells and viruses, led a study to find out how this happened. They found that 2 other mutations in the virus allowed it not only to evade the effects of Tamiflu but also to survive and spread. In addition, the mutations took place before the 3rd and final mutation allowing the virus to evade the drugs. This means that scientists can monitor flu viruses for the initial 2 mutations to give early warning that they are about to become drug resistant.

This is important in planning for both seasonal influenza and pandemics. Seasonal flu kills between 250,000 and 500,000 people every year globally. H1N1 'swine' flu may have been just slightly more deadly -- statistics will take years to gather -- but it affects younger adults and children in contrast to seasonal flu, which kills more elderly people. Currently 'swine flu' is easily treated by Tamiflu but that could change at any time. So doctors need drugs on hand to save lives and if one drug will be useless, they need to know that because flu must be treated within days of onset for treatment to be useful.

National, Research (NIH/NIAID [edited], June 15): Mice injected with a 2009 H1N1 pandemic influenza vaccine and then exposed to high levels of the virus responsible for the 1918 influenza pandemic do not get sick or die, report scientists funded by the National Institute of Allergy and Infectious Diseases. The new vaccine works against the old virus because the 1918 and the 2009 strains of H1N1 influenza share features that allow vaccine-generated antibodies to recognize both viruses. To learn more, similar challenge studies need to be conducted in other animals, including monkeys, but the investigators say their results suggest people who are vaccinated against 2009 H1N1 influenza or were exposed to the virus could have similarly cross-protective antibodies against the 1918 strain of H1N1. This finding, they add, should help allay concerns about the potential consequences of an accidental release of the 1918 influenza virus from high-containment laboratories or its possible use as a bioterror weapon.

Adolfo Garcia-Sastre, Ph.D., of Mount Sinai School of Medicine led the research. Groups of mice were exposed to lethal amounts of the 1918 influenza virus 14 or 28 days after receiving a 2009 H1N1 influenza vaccine; a seasonal H3N2 influenza vaccine (not designed to protect against H1N1 virus); or no vaccine. All of the 2009-H1N1-vaccinated mice survived. Unvaccinated mice and mice that received the H3N2 vaccine all died. (Mice vaccinated with a seasonal flu vaccine designed to protect against a 2007 strain of H1N1 were mostly protected from lethal challenge; 80 percent of mice in that group survived.)

The researchers also injected mice with blood serum taken from people who had received 2009 H1N1 influenza vaccine. The serum, which contained antibodies against 2009 H1N1 influenza virus, protected the mice from death when they were later exposed to the 1918 H1N1 influenza virus.

International, Human (WHO, June 8): The Ministry of Health in China has announced a new confirmed human case of H5N1 infection. The case is a 22-year-old pregnant female from Hubei Province. She had onset of symptoms on 23 May and died on 3 June. Investigations into the source of her infection indicate exposure to sick and dead poultry. Close contacts of the case are being monitored and to date all remain well. Of the 39 cases confirmed to date in China, 26 have been fatal.

International, Poultry (Thai News Service, June 9): A bird flu outbreak has been reported in central Quang Nam Province's Duy Xuyen District [Vietnam], said head of the district's animal health station Nguyen Van Hoa. Nearly 10,000 chickens infected with A/H5N1 were recently discovered. 50% of them had not been vaccinated, Hoa said. Authorities have implemented measures to prevent the spread of the disease, including sterilising breeding farms, culling infected chickens and setting up quarantine stations.

Michigan Wild Bird Surveillance (USDA, as of June 17): For the 2010 testing season (April 1, 2010-March 31, 2011), highly pathogenic avian influenza subtype H5N1 has not been recovered from 804 samples tested nationwide, including 3 Michigan samples (1 live wild bird, 2 hunter-killed birds). For more information, visit the National HPAI Early Detection Data System at <http://wildlifedisease.nbi.gov/ai/>.

To learn about avian influenza surveillance in Michigan wild birds or to report dead waterfowl, go to Michigan's Emerging Disease website at <http://www.michigan.gov/emergingdiseases>.

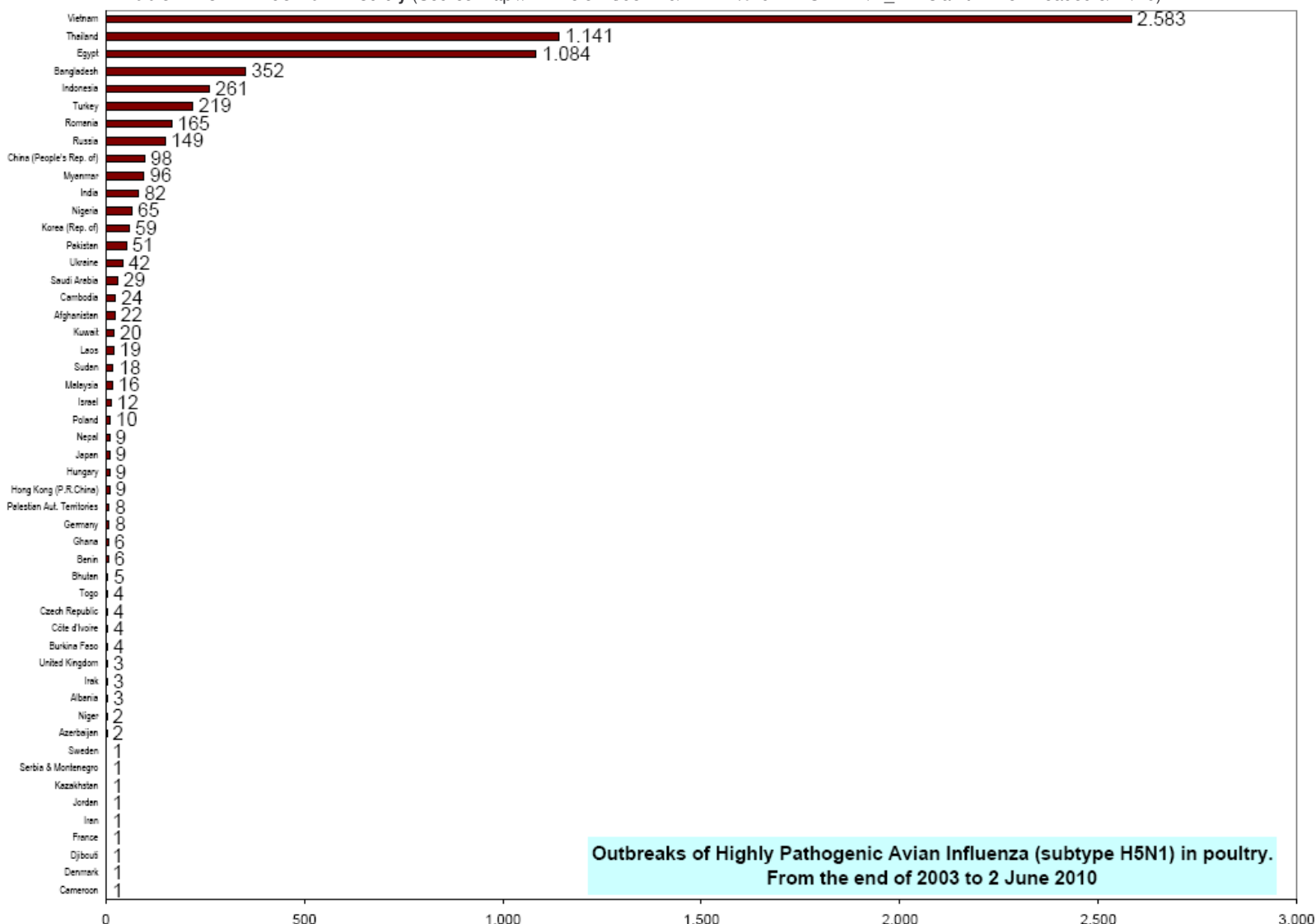
For questions or to be added to the distribution list, please contact Susan Peters at PetersS1@michigan.gov

Contributors

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Table 1. H5N1 Influenza in Poultry (Source: http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm Downloaded 6/14/10)



**Outbreaks of Highly Pathogenic Avian Influenza (subtype H5N1) in poultry.
From the end of 2003 to 2 June 2010**

Table 2. H5N1 Influenza in Humans - Cases up to May 6, 2010. http://www.who.int/csr/disease/avian_influenza/country/cases_table_2010_06_08/en/index.html. Downloaded 6/14/2010. Cumulative number of lab-confirmed cases reported to WHO. Total cases includes deaths.

| Country | 2003 | | 2004 | | 2005 | | 2006 | | 2007 | | 2008 | | 2009 | | 2010 | | Total | |
|----------------------------------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|
| | cases | deaths | cases | deaths | cases | deaths | cases | deaths | cases | deaths | cases | deaths | cases | deaths | cases | deaths | cases | deaths |
| Azerbaijan | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 5 |
| Bangladesh | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Cambodia | 0 | 0 | 0 | 0 | 4 | 4 | 2 | 2 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 10 | 8 |
| China | 1 | 1 | 0 | 0 | 8 | 5 | 13 | 8 | 5 | 3 | 4 | 4 | 7 | 4 | 1 | 1 | 39 | 26 |
| Djibouti | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Egypt | 0 | 0 | 0 | 0 | 0 | 0 | 18 | 10 | 25 | 9 | 8 | 4 | 39 | 4 | 19 | 7 | 109 | 34 |
| Indonesia | 0 | 0 | 0 | 0 | 20 | 13 | 55 | 45 | 42 | 37 | 24 | 20 | 21 | 19 | 3 | 2 | 165 | 136 |
| Iraq | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 2 |
| Lao People's Democratic Republic | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 |
| Myanmar | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Nigeria | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Pakistan | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 |
| Thailand | 0 | 0 | 17 | 12 | 5 | 2 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 25 | 17 |
| Turkey | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 4 |
| Viet Nam | 3 | 3 | 29 | 20 | 61 | 19 | 0 | 0 | 8 | 5 | 6 | 5 | 5 | 5 | 7 | 2 | 119 | 59 |
| Total | 4 | 4 | 46 | 32 | 98 | 43 | 115 | 79 | 88 | 59 | 44 | 33 | 73 | 32 | 31 | 13 | 499 | 295 |